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ANALYSIS OF COMPARISON OF PREGNANCY OUTCOMES IN INFERTILE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME USING LETROZOLE

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Abstract:

Introduction: *The polycystic ovary syndrome, which is diagnosed on the basis of hyperandrogenism, oligo ovulation with associated oligomenorrhea, and polycystic ovaries on ultrasonography, affects 5 to 10% of reproductive-age women and is the most common cause of anovulatory infertility.* ***Objectives of the study:*** *This present study aimed to investigate the efficacy of letrozole in comparison with Clomiphene citrate in local population of Pakistan.* ***Study design:*** *This was a prospective study conducted at DHQ hospital Gujranwala during 2016 to 2017. This study was based on the local female population of Pakistan. Total number of selected patients was 50. This study was done according to the rules and regulations of ethical committee of hospital. The patients were selected from the outpatient department of Obstetrics and Gynecology by the researcher.* ***Results:*** *A total of 100 patients with the polycystic ovary syndrome were randomly assigned to a treatment group and the two groups were well matched at baseline. The mean age in this study is 28 years. In Group A, the BMI is 35.1 and in group B the mean BMI is 35.2In the age group 25-29 years, in group B (Clomiphene Citrate), treatment was found to be efficacious in 24.5% patients, while it was efficacious in 48.1% (n=26/54) in group A (Letrozole) patients. Having a significant p-value 0.013 (<0.05), implying significant better results with Letrozole in terms of successful pregnancies.* ***Conclusion:*** *In conclusion, our study showed that letrozole was superior to clomiphene as a treatment for an ovulatory infertility in women with the polycystic ovary syndrome. Letrozole was associated with higher live-birth and ovulation rates.*

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INTRODUCTION:

The polycystic ovary syndrome, which is diagnosed on the basis of hyperandrogenism, oligo-ovulation with associated oligomenorrhea, and polycystic ovaries on ultrasonography, affects 5 to 10% of reproductive-age women and is the most common cause of an ovulatory infertility [1]. Despite the fact that the disorder is a complex regenerative metabolic issue, the hypothalamic pituitary hub has been the objective of first-line ovulation-acceptance treatment. Clomiphene citrate, a particular estrogen-receptor modulator that estranges the negative input of estrogen at the hypothalamus with a resulting increment in ovarian incitement by endogenous gonadotropin, has been utilized for this sign for quite a long time [2]. Fruitlessness is regular in youthful females with polycystic ovarian disorder. Distinctive treatment choices are accounted for in the writing for ovulation enlistment.

Polycystic ovarian disorder is a much of the time happening confusion of female Endocrinopathy. Its prevalence has more noteworthy variety as for indicative criteria utilized. The prevalence ranges from 3% to 20%. There are numerous highlights demonstrating the presence of Polycystic ovarian disorder with most usually displaying attributes like raised clinical and research center records of androgen levels alongside polycystic ovaries on ultrasound [3]. The patients likewise give irregular ovulation indications. The clinical introduction incorporates anomaly in menstrual cycle, hirsuitism, fruitlessness, stomach heftiness, hypertension and additionally industrious skin break out and androgen-subordinate alopecia [4]. Insulin resistance happens freely and all the more as often as possible because of stoutness. The blend of both polycystic ovarian disorder and stoutness firmly irritate the insulin affectability. There are a few medications which are utilized as ovulation enlistment specialists in ladies having the polycystic ovarian disorder [5]. The most normally and ideally utilized medication is clomiphene citrate (CC), which is an estrogen receptor modulator and much of the time utilized as a part of polycystic ovarian disorder ladies from numerous years. It has numerous points of interest of utilization like it has less cost and has more prominent wellbeing profile rather than different medications utilized for this reason. Another fundamental preferred standpoint is its practicality of oral organization [6].

Objectives of the study

This present study aimed to investigate the efficacy of letrozole in comparison with Clomiphene citrate in local population of Pakistan.

Study design

This was a prospective study conducted at DHQ hospital Gujranwala during 2016 to 2017. This study was based on the local female population of Pakistan. Total number of selected patients was 100. This study was done according to the rules and regulations of ethical committee of hospital. The patients were selected from the outpatient department of Obstetrics and Gynecology by the researcher.

Data collection

The inclusion criteria included patients in the age group of 20-35 years with PCOS and having infertility for more than one year. Patients with hyperprolactinemia, thyroid disorder, male factor, suspected tubal factor, endometriosis, unexplained infertility were not included in the study. Similarly, patients having Uterine and adnexal pathology e.g. leiomyomata, Hyperprolactinemia, FSH>9 ml U/ml (during early follicular phase), peritonitis, genital tuberculosis as per history and/ or having an abnormal pelvic anatomy were not selected in the study.

Sampling

All the women were randomly divided into two equal groups of 50 patients. In group, A clomiphene citrate 50 mg was given and in group B letrozole 2.5mg was given. Patients followed with follicle monitoring with Ultrasound on day 8 of the menstrual cycle, endometrial thickness was determined at the greatest diameter. The final outcome measure or efficacy of the drug was measured in terms of conception within three cycles. Basic demographic information including name, age duration of marriage was recorded on a predesigned proforma.

Statistical analysis

All the collected data was entered and analyzed through Statistical Package for social sciences

(SPSS version 21). Quantitative variables were expressed as Mean ± SD. Qualitative variables were presented as frequency and percentages. Chisquare test was used to compare final outcome (efficacy) between two groups. P-value<0.05 was considered as statistically significant.

RESULTS:

A total of 100 patients with the polycystic ovary syndrome were randomly assigned to a treatment group and the two groups were well matched at baseline. The mean age in this study is 28 years. In Group A, the BMI is 35.1 and in group B the mean BMI is 35.2. When the study sample was stratified with respect age it was found that there was no

significant (p value > 0.05) in the age group 20-24 years, when the efficacy of Clomiphene Citrate was compared with Letrozole group patients. In the age group 25-29 years, in group B (Clomiphene Citrate), treatment was found to be efficacious in 24.5% patients, while it was efficacious in 48.1% (n=26/54) in group A (Letrozole) patients. Having a significant p-value 0.013 (<0.05), implying significant better results with Letrozole in terms of successful pregnancies. In the age group 30-35 years, in group B (Clomiphene Citrate), treatment was not efficacious in any patient, while it was efficacious in

20.0% in group A (Letrozole) patients having a p-value of 0.041 (<0.05), implying significantly higher rates of successful pregnancies. The stratification on the basis of infertility duration is shown in table 02.

Table 01: demographic characteristics of patients

Characteristics	Letrozole group	Clomiphene Citrate group
Age — yr	28.8±4.0	28.9±4.5
Body-mass index†	35.1±9.0	35.2±9.5
Ferriman–Gallwey hirsutism score‡	16.9±8.5	17.0±8.6
Race or ethnic group — no. (%)§		
White	302 (80.3)	288 (77.0)
Black	44 (11.7)	56 (15.0)
Asian	12 (3.2)	12 (3.2)
Mixed race	12 (3.2)	15 (4.0)
Hispanic or Latino	68 (18.1)	60 (16.0)
Fertility history		
Duration of time attempting to conceive — mo	42.5±37.6	40.9±38.0
Previous live birth — no. (%)	73 (19.4)	75 (20.1)
Ultrasonographic findings		
Antral follicle count in both ovaries	46.5±28.5	47.4±27.4
Polycystic ovaries according to modified Rotterdam criteria — no./total no. (%)¶	349/374 (93.3)	354/369 (95.9)

Table 02: Analysis of outcomes of patients

Outcomes	Letrozole group	Clomiphene Citrate group	Diff B/W groups	95%CI	p-value
Primary outcome					
Live birth — no. (%)	72 (19.1)	103 (27.5)	8.4 (2.4 to 14.4)	1.44 (1.10 to 1.87)	0.007
Singleton live birth — no./total no. (%)	67/72 (93.1)	99/103 (96.1)	3.1 (–3.9 to 10.0)	1.03 (0.96 to 1.11)	0.49
Twin live birth — no./total no. (%)§	5/72 (6.9)	4/103 (3.9)	–3.0 (–10.0 to 3.9)	0.56 (0.16 to 2.01)	0.49
Birth weight					
No. of infants	71	102			
Mean weight — g	3229.9±715.3	3232.3±657.4	2.4 (–205.6 to 210.4)		0.83
Sex ratio at birth (boys:girls)	0.88 (36:41)	0.65 (42:65)		0.74 (0.41 to 1.33)¶	
Duration of pregnancy					
No. of women	72	101			
Mean duration — wk	38.0±3.6	38.4±2.7	0.4 (–0.6 to 1.4)		0.59
Secondary outcomes					
Pregnancy					
Conception — no. of women (%)	103 (27.4)	154 (41.2)	13.8 (7.1 to 20.5)	1.50 (1.23 to 1.84)	<0.001
Pregnancy — no. of women (%)	81 (21.5)	117 (31.3)	9.7 (3.5 to 16.0)	1.45 (1.14 to 1.85)	0.003
Twin pregnancy — no. of women/ total no. of pregnancies (%)	6/81 (7.4)	4/117 (3.4)	–4.0 (–10.6 to 2.6)	0.46 (0.13 to 1.58)	0.32
Time to pregnancy‖					
No. of women	90	145			
Mean time — days	85.9±48.8	90.4±44.4	4.5 (–8.0 to 17.0)		0.27
Pregnancy loss					
Pregnancy loss among women who conceived — no./total no. (%)	30/103 (29.1)	49/154 (31.8)	2.7 (–8.7 to 14.1)	1.09 (0.75 to 1.60)	0.65
Loss in first trimester — no./ total no. (%)	29/103 (28.2)	45/154 (29.2)	1.1 (–10.2 to 12.3)	1.04 (0.70 to 1.54)	0.85
Ovulation					
Women who ovulated — no. (%)	288 (76.6)	331 (88.5)	11.9 (6.5 to 17.3)	1.16 (1.08 to 1.24)	<0.001
No. of ovulations/total treatment cycles (%)	688/1425 (48.3)	834/1352 (61.7)	13.4 (9.7 to 17.1)	1.28 (1.19 to 1.37)	<0.001

DISCUSSION:

We found that letrozole was more effective as a fertility treatment than clomiphene in women with the polycystic ovary syndrome [7]. Ovulation, origination, pregnancy, and live birth were fundamentally more probable after treatment with letrozole. The rate of pregnancy misfortune, the mean pregnancy length and birth weight, and rates of neonatal difficulties (counting oddities) did not vary essentially between treatment gatherings [8]. In spite of the fact that the twin pregnancy rate was bring down with letrozole than with clomiphene, our examination was underpowered to identify a critical between-gather distinction (23% power with an alpha level of 0.05). The general birth-deformity rate was comparative in the two treatment gatherings, however there were four noteworthy inherent peculiarities in the letrozole gathering and one in the clomiphene gathering; this distinction was not huge but rather given the gathering size, we can't preclude a potential contrast [8].

The two medications utilized as a part of our examination have been assigned by the FDA as pregnancy class X (despite the fact that clomiphene is endorsed for ovulation enlistment). The abnormality composes seen with letrozole in our examination are various, a finding that contends against a typical instrument[9]. Besides, the oddity rates are lower than those announced in a vast population-based examination in Pakistan that inspected birth-deformity rates after any methods for helped multiplication or ovulation acceptance [9]. We hypothesize that the higher rates in Pakistan may be because of a set up national birth-abandons registry with obligatory announcing of all oddities recognized during childbirth or inside the neonatal period. We analyzed the pregnancy, birth, and neonatal records of every single live birth; furthermore, right around

three fourths of the neonates experienced physical examination by restorative work force prepared in identifying inborn peculiarities[10]. Our information show that inconsistency rates are comparable with the two medicines we assessed and these rates are likewise like the rate in a population of healthy, fruitful ladies who considered without experiencing treatment for helped propagation [11]. The live-birth rate was higher with letrozole than with clomiphene among ladies with the polycystic ovary disorder in our examination. Earlier preliminaries seem to have been inadequately controlled to distinguish contrasts in live-birth rates, needed satisfactory covering of study-aggregate assignments, or did not take into consideration rehashed cycles to accomplish an ovulatory reaction with an expanded measurements [12]. Two very much outlined, industry-supported, multicenter, stage 2 ponders, both of which were randomized, twofold visually impaired, measurements discovering, noninferiority thinks about, contrasted anastrozole and clomiphene in ladies with oligo-ovulation (a large portion of whom had the polycystic ovary disorder), with ovulation as the essential result. The two investigations reasoned that treatment with anastrozole was less powerful than a 5-day course of clomiphene[10]. The discrepant results with comparative medications may mirror the more prominent concealment of aromatase with letrozole than with anastrozole.16 When given to ladies with a background marked by bosom growth who were experiencing ovarian incitement with gonadotropins, letrozole was related with essentially bring down estradiol levels amid treatment than was anastrozole in a zone under-the bend investigation [13].

CONCLUSION:

In conclusion, our study showed that letrozole was superior to clomiphene as a treatment for an ovulatory infertility in women with the polycystic ovary syndrome. Letrozole was associated with higher live-birth and ovulation rates.

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